Microbiology of Urogenital system

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Genital infections encompasses a variety of clinical entities, including:

- Bacterial vaginosis
- Chancroid
- Gonorrhoea
- Chlamydia
- Syphilis
- *Mycoplasma genitalium*
- Trichomoniasis
- Vulvovaginal candidiasis
- Genital warts
- Human immunodeficiency virus.
- Genital herpes
Symptoms and signs of disease may include vaginal discharge, penile discharge, ulcers on or around the genitals, and pelvic pain. Dysuria and dyspareunia can also happen. Many STDs can be asymptomatic.

Patients with one STI should be assessed for the presence of others, because of similar risk factors and vulnerability of an inflamed genital epithelium to other infections.

Risk factors include:

- The number of sexual partners and frequency of partner change
- Failure to use barrier contraception,
- Lower socioeconomic status,
- Age <25 years
- Symptomatic partner,
- Sexual orientation (syphilis, gonorrhoea, HIV, and hepatitis B are more prevalent amongst MSM in the UK), and sexual practices (orogenital and anogenital contact).
In 2012, among women aged 15–49 years, the estimated global prevalence of chlamydia was 4.2% (3.7–4.7%), gonorrhoea 0.8% (0.6–1.0%), trichomoniasis 5.0% (4.0–6.4%), and syphilis 0.5% (0.4–0.6%); among men, estimated chlamydia prevalence was 2.7% (2.0–3.6%), gonorrhoea 0.6% (0.4–0.9%), trichomoniasis 0.6% (0.4–0.8%), and syphilis 0.48% (0.3–0.7%). Prevalence and incidence estimates varied by region and sex.

Nearly one million new infections with curable STI each day.
Prevalence of sexually transmitted infections among sexually active Jordanian females.

Mahafzah AM, Al-Ramahi MQ, Asa'd AM, El-Khateeb MS.

RESULTS: The prevalence of C. trachomatis infection was 0.6% and 0.5%, among symptomatic and asymptomatic women respectively, that of N. gonorrhoeae was 0.9% and 2.2%, that of T. pallidum 0.0% and 0.0%, and that of Tr. vaginalis was 0.7% and 0.5%. These prevalence rates did not differ significantly between symptomatic and asymptomatic women.

CONCLUSIONS: Based on the low prevalence of sexually transmitted infections detected in this study among Jordanian women, the need for screening programs for such infections is questioned.
Bacterial vaginosis / etiology

• Bacterial vaginosis (BV) is a common cause of unusual vaginal discharge. BV isn't a sexually transmitted infection (STI), but it can increase your risk of getting an STI such as chlamydia.

• Normal vaginal flora appears dominated by one or two species of Lactobacillus. Rather than being due to a single organism, BV is caused by complex changes in the balance of the microbiological flora.

• Lactobacilli produce H2O2 which lowers the pH— the loss of these organisms permits an increase in pH and overgrowth of vaginal anaerobes (e.g. Bacteroides, Mobiluncus).

• The newly found bacterial species degrade vaginal peptides into offensive-smelling products and promote discharge and exfoliation of the epithelial layers.
Bacterial vaginosis / epidemiology / signs and symptoms

- Worldwide prevalence ranges from 11% to 48% in women of childbearing age.

- Risk factors for acquisition—new or multiple sexual partners, vaginal douching, smoking. It can occur in women who have never had vaginal intercourse.

- 50 to 75% of cases are asymptomatic. In symptomatic cases, there is thin, white, fishy smelling discharge, most noticeable after intercourse.

- Pregnant women with BV have a higher rate of preterm delivery and pregnancy complications.

- BV also increases the risk of contracting other STDs like HIV.
The diagnosis of BV is usually based on **Amsel criteria**. The first three findings are sometimes also present in patients with trichomoniasis;

- homogeneous, **watery, white-grey discharge** coating the vaginal walls;

- **vaginal pH > 4.5**;

- positive amine test— add 10% KOH to a sample of discharge— positive if produces a **fishy odour**;

- the presence of ‘**clue cells**’ (epithelial cells studded with adherent coccobacilli) on a saline wet mount— the single best predictor of BV.
• Infection **resolves spontaneously** in one-third of cases.

• Treatment may **reduce the risk of acquiring other STDs.** And includes: **metronidazole**— 500mg bd PO for 7 days or **clindamycin**— 300mg bd PO for 7 days

• Thirty per cent of **patients experience recurrence** within 3 months. A prolonged (e.g. 14 days) or alternative treatment course should be used in such patients.
Trichomoniasis / etiology

- An STI caused by the flagellated protozoan *T. vaginalis* (TV).

- TV pathogenesis include damage to host tissue mediated by parasite **killing of host cells**, **disruption** of steady-state **vaginal microbial ecology**, and eliciting inflammation by **activating the host immune response**.

![Diagram of Trichomonas vaginalis](image)
Trichomoniasis / epidemiology/ signs and symptoms

- Transmission is by sexual contact, and its incidence is highest in women with multiple sexual partners and those with other STIs.

- Infection is asymptomatic in 10–50% of women and 15–50% of men.

- Symptoms include frothy, yellow vaginal discharge (may be itchy and smelly), dyspareunia, dysuria, and lower abdominal pain.

- Punctate haemorrhages on the cervix (‘strawberry cervix’) in 2% of patients.

- Can lead to urethritis in men.
Bacterial vaginosis / diagnosis and treatment

- **Microscopy**— phase-contrast or dark-ground microscopy of wet preparation of genital specimens will demonstrate the **motile flagellated protozoans** in 48–80% of infected women and 50–90% of infected men.

- Point-of-care tests, e.g. OSOMR *Trichomonas* rapid test has a sensitivity of 80–94% and a specificity of >95%.

- **NAATs** offer the highest sensitivity and are becoming the gold standard

- **Metronidazole** 2g stat dose or tinidazole 2g stat dose. Partners and asymptomatic individuals should be treated
Spirochetes are thin, helical gram-negative bacteria. The most important treponemal species that causes human disease is *Treponema pallidum,* the causative agent for Syphilis.

*T. pallidum* has not been cultured regularly in vitro because they are dependent on host cells for many metabolites (e.g. purines, pyrimidines, amino acids). Moreover, they’re extremely sensitive to oxygen (microaerophilic or anaerobic).

**FIGURE 32-3** *Treponema pallidum* in the direct fluorescent antibody test for *T. pallidum.* (From Morse SA, Ballard RC, Holmes KK)
• Between 2000 and 2012, the incidence of newly acquired disease has **increased** each year.

• Patients infected with syphilis are at **increased risk for transmitting and acquiring HIV** when genital lesions are present.

• **Syphilis cannot be spread through contact with inanimate objects** such as toilet seats (since the bacteria is very labile to drying and disinfectants). The most common route of spread is by **direct sexual contact**.

• Other routes include **congenitally** (from an infected mother) or by **transfusion** with contaminated blood.
The clinical course of syphilis evolves through three phases. If the patient is not treated, syphilis cause systemic devastating damage.

**primary phase** is characterized by skin lesions (chancres) at the site where the spirochete penetrated. In the **secondary phase**, the clinical signs of disseminated disease appear, (e.g. skin lesions over the entire body, fever, headache). Symptoms resolve within weeks.

Late syphilis severely damages organs involved (e.g., neurosyphilis, tabis dorsalis, cardiovascular syphilis) leading to various symptoms (e.g. dementia or blindness).
The Stages of Syphilis

Primary

The chancre lesion is the hallmark of primary syphilis. It may appear 10-90 days after exposure. Common sites include penis and labia. Other sites include anus, oral mucosa. Without treatment, chancre disappears in 2-8 weeks.

Secondary

Rash, pink to brown macules. Involves palms/soles in 50% of cases.

Oral lesions called "mucous patches" resembling snail tracks.

Ocular syphilis manifestations including anterior or posterior uveitis.

Genital-inguinal rashes, including tinea-mimicker or heaped-up wart-like lesions called condyloma lata.

Latent

Latent syphilis refers to asymptomatic infection after the period of primary and secondary syphilis (noticed or unnoticed) has passed.

Early Latent

Early latent refers to asymptomatic patients with positive testing, in whom history can confirm exposure to or symptoms of primary or secondary syphilis within the last year. This group may receive single-dose penicillin like primary or secondary.

Latent syphilis refers to asymptomatic infection after the period of primary and secondary syphilis (noticed or unnoticed) has passed.

Late Latent

Late latent patients have positive serology but do not meet criteria for early. Thus, multiple doses of penicillin.

Late (Tertiary)

Late Neurosyphilis, including tabes dorsalis, gait impairments, and dementia. Tabes dorsalis damages the dorsal columns and sensory nerve roots, causing a syndrome of pain and sensory deficits similar to those of B12 deficiency.

Gumma are ulcerating granulomas on skin, bone, and internal organs.

Cardiovascular effects of late syphilis include aortic aneurysm and coronary arteritis.
Syphilis / diagnosis and treatment

• **Darkfield microscopy, immuno-fluorescent stains, or PCR** can be used on immediate samples (from a chancre) for visualization and diagnosis.

• Serology is the most important tool;

  **non- treponemal/ cardiolipin tests**, e.g. venereal disease research laboratory (VDRL)/ Rapid plasma regain test (RPR). A quantitative test should be done to **screen**, stage the disease and monitor treatment.

  **specific treponemal tests** *Treponema pallidum* particle agglutination (**TP-PA**) test can be used for **diagnosis**

• Syphilis be controlled only through the practice of **safe-sex** techniques and adequate treatment with antibiotics

• **Penicillin** is the drug of choice. (Benzathine benzylpenicillin / Penicillin G).
Gonorrhoea / etiology

- A **purulent infection** of mucous membranes (e.g. urethra, rectum, cervix, conjunctiva, pharynx) caused by *N. gonorrhoeae*.

- *Neisseria* species are aerobic **gram-negative** bacteria, typically coccoid shaped arranged in pairs (**diplococci**)

- The presence of *N. gonorrhoeae in a clinical specimen is always considered significant*. In contrast, strains of *N. meningitidis* can **colonize the nasopharynx of healthy people** without producing disease.

- *N. gonorrhoeae is fastidious and only grows on enriched chocolate agar** and other supplemented media.
It is the second commonest STI in the UK, affecting predominantly young people (peaking in males aged 20–24 years and females aged 16–19 years. The recent increase in incidence and **growing prevalence of antimicrobial resistance** have made it a major public health concern.
Gonorrhoea / pathophysiology

1. Adherence to urogenital epithelium
   - N. gonorrhoeae
   - Opa protein
   - Type IV pili

2. Competition with resident microbiota, nutrient acquisition and microcolony formation
   - Microbiota

3. Colonization and invasion of epithelium
   - Peptidoglycan
   - OMV
   - LOS

4. Cytokine, chemokine and inflammatory transcription factor activation
   - Macrophage

5. Peptidoglycan, LOS and OMVs cause NOD and TLR activation on epithelial cells, macrophages and DCs; HBP causes activation of TIFA-dependant innate immunity in epithelial cells and macrophages

6. Influx of neutrophils; adherence and phagocytosis of N. gonorrhoeae

7. A neutrophil-rich, purulent exudate facilitates transmission

Urogenital epithelium

Transcytosis

DC

NLR

TLR

Cytokine
Chemokine
Gonorrhoea / signs and symptoms

- Genital infection in men is primarily restricted to the urethra. A purulent urethral discharge and dysuria develop after a 2- to 5-day incubation period. Virtually all infected men have acute symptoms.

- As many as half of all infected women have mild or asymptomatic infections.

- Retrograde spread may occur, causing salpingitis/ endometritis, PID, and tubo-ovarian abscesses in up to 20% of women with cervicitis.

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**Neisseria gonorrhoeae**

**Gonorrhea:** characterized by purulent discharge for involved site (e.g., urethra, cervix, epididymis, prostate, rectum) after 2- to 5-day incubation period

**Disseminated infections:** spread of infection from genitourinary tract through blood to skin or joints; characterized by pustular rash with erythematous base and suppurative arthritis in involved joints

**Ophthalmia neonatorum:** purulent ocular infection acquired by neonate at birth
Gonorrhoea / diagnosis and treatment

• Samples include **Exudates** (by a swab into urethra), **urine**, **cervical or throat swabs**

• **Microscopy**— provides rapid, near-patient diagnosis in symptomatic patients and shows **Gram-negative diplococci** within polymorphonuclear cells.

• **Culture**— all infected areas should be swabbed and plated onto selective media, both to confirm diagnosis and to provide antibiotic susceptibility data.

• **Nucleic acid amplification tests** (NAATs)— these have become the screening test of choice for asymptomatic individuals with urethral and endocervical infection, and for rectal and pharyngeal infection in MSMs.

• Treatment should include **patient and sexual partner/s**.

• First-line therapy is **ceftriaxone** 500mg IM single dose plus **azithromycin** 1g PO single dose
Chlamydia / etiology

- A common STD caused by **Chlamydia trachomatis**. An **obligate intracellular parasites**, 0.3 microm in diameter, with a unique life cycle.

- Infects epithelial cells, which are found on the mucous membranes of **the urethra, endocervix, endometrium, fallopian tubes, anorectum, respiratory tract, and conjunctivae**

- Metabolically inactive **infectious forms** (**elementary bodies [EBs]**) and metabolically active **noninfectious forms** (**reticulate bodies [RBs])**.
Chlamydia / epidemiology

- Chlamydia infections are the **most common bacterial sexually transmitted diseases** in humans and are **the leading cause of infectious blindness** worldwide.

- Other than **sexual transmission**, **eye-to-eye transmission** of trachoma is by **droplet, hands, contaminated clothing**, and flies that transmit ocular discharges from the eyes of infected children to the eyes of uninfected children.

- **Trachoma** is the **leading cause of preventable blindness**. Infections occur predominantly in children, who are the chief reservoir of *C. trachomatis* in endemic areas.
Most genital tract infections in **women** are **asymptomatic** (as many as 80%) while most in **men** are **symptomatic**, as many as 25% of the infections will be inapparent.

Infection may **persist** for many years if untreated, infection can spread to the upper genital tract in women causing **pelvic inflammatory disease** which may result in future infertility or ectopic pregnancy.

It can cause **cervicitis** in women and **urethritis** and **proctitis** in both men and women.

Other presentations— **Lymphogranuloma venereum** (LGV) (the cause of 10% of genital ulcers in tropical countries)
Chlamydia / diagnosis and treatment

• Samples include **Exudates** (by a swab into urethra), **first catch urine**, **cervical or throat swabs**

• **Culture**— not routinely recommended, with low sensitivity and expensive.

• **Nucleic acid amplification tests** (NAATs)— these have become the diagnostic test of choice, as they are highly sensitive (90–95%).

• Treatment should include **patient and sexual partner/s**.

• The drug of choice for reasons of compliance is **doxycycline** 100mg bd PO for 7 days or **azithromycin** 1g single dose
Nongonococcal urethritis caused by Mycoplasma

- **Mycoplasma** and **Ureaplasma** organisms are the **smallest free-living bacteria**. They are unique among bacteria because they **do not have a cell wall** and their cell membrane contains **sterols**.

- **M. genitalium** and **Ureaplasma urealyticum** can cause **nongonococcal urethritis** (NGU) and **pelvic inflammatory disease**.
Nongonococcal urethritis caused by Mycoplasma

- The most sensitive diagnostic tests are **PCR amplification** tests of species-specific gene targets.

- Absence of the cell wall renders the mycoplasmas resistant antibiotics that interfere with synthesis of the cell wall (e.g. Penicellins).

- Rising incidence and emerging antimicrobial resistance are a major concern these days.

- The poor clinical outcomes with **doxycycline** therapy led to the use of **azithromycin** as the primary drug of choice.
Vulvovaginal candidiasis / etiology

- Candidiasis is an infection caused by **Candida albicans**, which is an opportunistic pathogenic yeast that is a common member of the human **gut flora**.

- **Candida** spp. may be found in the lower genital tract of 10–20% of asymptomatic women.

- 29–49% of premenopausal women reporting at least one episode of candidiasis.

- Candidal infection is uncommon in prepubertal women.
C. albicans is the cause of 80–92% of cases, but the incidence of other Candida spp., such as C. glabrata can occur.

Recurrent infection—defined as ≥4 episodes a year and seen in 5–8% of women. Susceptibility seems to be largely determined genetically.
Vulvovaginal candidiasis / diagnosis and treatment

- wet mount of the discharge with 10% KOH may allow recognition of yeast and hyphae, but microscopy is negative in around 50%.

- Self-diagnosis unreliable— one study demonstrated that only 34% of those women self-diagnosing candidal infection actually had it.

- Vaginal pH is around 4–4.5 (unlike trichomonal infection or BV).

- Perform culture in patients with persistent discharge or recurrent symptoms unresponsive to azole treatment.
90% of cases represent uncomplicated infections (healthy, non-pregnant women with mild/moderate symptoms, infrequent episodes and infection with *C. albicans*).

Oral and topical treatments are similarly effective, with topical therapy relieving symptoms more rapidly, but oral being preferred by women, e.g. PO fluconazole.

The immunosuppressed and those with severe symptoms are unlikely to respond to short treatment courses—7–14 days of topical therapy is recommended.

Pregnancy—treat only for symptoms using a topical imidazole for 7–14 days (e.g. clotrimazole). Oral azoles are contraindicated in pregnancy.
A 26-year-old male patient came to the dermatology clinic of Tanta University hospital complaining from severe burning sensation during urination and dysuria for 4 days. Additionally, he was suffering from penile discharge and testicular tenderness. He had a history of multiple heterosexual relationships with a last contact 8 days ago. On physical examination, vital signs showed: blood pressure 110/79, pulse 75, and temperature 37.6°C. There was mucopurulent cloudy discharge from urethra. Swollen testicles were also observed. When the patient asked about any other symptoms, he mentioned feeling fatigue with pain in the knee joints and ankles 2 weeks ago but he did not receive any medical remedy until the appearance of severe irritation, redness in the eye, as well as edema in the eyelid with the presence of copious discharge (conjunctivitis). These symptoms seem to be unrelated to a degree that may obscure the diagnosis.
The results of susceptibility testing were interpreted according to CLSI. It revealed multiple drug resistance to ampicillin, ampicillin/clavulanic acid, cephradine, cefotaxime, cefepime, cefuroxime, ceftriaxone, ciprofloxacin, chloramphenicol, sulfamethoxazole, trimethoprim, tetracycline, doxycycline, and spectinomycin. Only gentamicin, rifampicin, and azithromycin were active against the test pathogen.
History

- 17-year-old white female
- College student
- Seeking advice about contraception
- Shy talking about her sexual practices
- Has never had a pelvic exam
- Has had two sex partners in past six months
- Does not use condoms or any other contraceptives
- Her periods have been regular, but she has recently noted some spotting between periods. Last menstrual period was 4 weeks ago.
- Denies vaginal discharge, dyspareunia, genital lesions, or sores

Physical examination

- Vital signs: blood pressure 118/68, pulse 74, respiration 18, temperature 37.1°C
- Breast, thyroid and abdominal exam within normal limits
- The genital exam reveals normal vulva and vagina
- The cervix appears inflamed, bleeds easily with swab insertion for diagnostic testing, and there is a purulent discharge coming from the cervical os.
- The bimanual exam is normal without cervical motion pain, uterine or adnexal tenderness.
3. Which laboratory tests should be ordered or performed?

- Pregnancy test
- Test for *Chlamydia trachomatis*
- Test for *Neisseria gonorrhoeae*
- Syphilis screen with RPR or VDRL
- Saline wet mount, pH and KOH preparation of vaginal secretions
- Counseling and testing for HIV
Laboratory Test Results for Suzy Jones

- NAAT for *Chlamydia trachomatis*: positive
- NAAT for *Neisseria gonorrhoeae*: negative
- RPR: non-reactive
- Wet mount: pH 4.2, no clue cells or trichomonads but numerous white blood cells (WBCs)
- KOH preparation: negative for "whiff test"
- HIV antibody test: negative
- Pregnancy test: negative
A 39-year-old man presented to the emergency department reporting several weeks of generalized weakness, headache, nausea, and migratory arthralgia. The patient had exclusively had sex with men, had participated in condomless anal insertive and receptive intercourse, and had been in a monogamous relationship during the past 6 months.

Physical examination revealed a painful ulcerated plaque on the upper lip, a macular rash with three crater-like scarred painless lesions (considered to be healing chancre) on the glans, a nonpruritic hyperkeratotic maculopapular palmar rash and bilateral submandibular lymphadenopathy. No alopecia, gummas, neurologic deficits or ocular or cardiovascular abnormalities were noted.

Ulcerated plaque on the upper lip. Results of laboratory testing included a positive reactive syphilis immunoglobulin G (IgG) enzyme immunoassay and a positive rapid plasma reagin (RPR) test (titer 1:256). Human immunodeficiency virus (HIV) testing was negative, and serologic testing demonstrated prior immunization to hepatitis B virus. Given the clinical presentation and laboratory findings, secondary syphilis was considered the most probable diagnosis.

The patient was treated with benzathine penicillin G 2.4 million units intramuscularly.
Clinical Case 23-1  Gonococcal Arthritis

Gonococcal arthritis is a common presentation of disseminated *Neisseria gonorrhoeae* infection. Fam and associates *(Can Med Assoc J 108:319–325, 1973)* described six patients with this disease, including the following patient, who has a typical presentation. A 17-year-old girl was admitted to the hospital with a 4-day history of fever, chills, malaise, sore throat, skin rash, and polyarthralgia. She reported being sexually active and having a 5-week history of a profuse yellowish vaginal discharge that was untreated. Upon presentation, she had erythematous maculopapular skin lesions over her forearm, thigh, and ankle, and her metacarpophalangeal joint, wrist, knee, ankle, and midtarsal joints were acutely inflamed. She had an elevated leukocyte count and sedimentation rate. Cultures of her cervix were positive for *N. gonorrhoeae*, but blood specimens, exudates for the skin lesions, and synovial fluid were all sterile. The diagnosis of disseminated gonorrhea with polyarthritis was made, and she was successfully treated with penicillin G for 2 weeks. This case illustrates the limitations of culture in disseminated infections and the value of a careful history.
History

Tanya Walters is a 24-year-old single female who presented at her clinic with complaints of a smelly, yellow vaginal discharge and slight dysuria for one week.

- Denies vulvar itching, pelvic pain, or fever
- Has had 2 sex partners over the past 6 months—did not use condoms with these partners—on oral contraceptives for birth control
- No history of sexually transmitted diseases, except for trichomoniasis one year ago
- Last check-up one year ago

Physical Exam

- Vital signs: blood pressure 112/78, pulse 72, respiration 15, temperature 37.3° C
- Cooperative, good historian
- Chest, heart, breast, musculoskeletal, and abdominal exams within normal limits
- No flank pain on percussion
- Normal external genitalia with a few excoriations near the introitus, but no other lesions
- Speculum exam reveals a moderate amount of frothy, yellowish, malodorous discharge, without visible cervical mucopus or easily induced cervical bleeding
- Bimanual examination was normal without uterine or adnexal tenderness
Laboratory Results

Vaginal pH—6.0
Saline wet mount of vaginal secretions—numerous motile trichomonads and no clue cells
KOH wet mount—negative for budding yeast and pseudohyphae
A patient has been diagnosed with primary syphilis (Stage I). When assessing the patient, which of these findings will the healthcare provider anticipate?

Choose 1 answer:

- **A** Reddish rash on the palms of the hands
- **B** Firm and painless genital ulcers
- **C** Sore throat and swollen lymph glands
- **D** Muscle weakness and visual changes
Further reading:

- Oxford handbook of infectious diseases and microbiology- Part 4: Clinical syndroms
  Chapter 18: Sexually transmitted infections

- Harrison's Infectious Diseases 3rd Edition
  SECTION III Infections in organ systems
  Chapter 35